REMARKS

Upon entry of the current amendments, claims 24-56, 59-61, 64-79, 81-83, and 85-104 will be pending in this application. Applicants thank the Examiner for allowing claims 24-39. Claims 57, 58, 62, 63, 80 and 84 have been canceled and claims 40-43, 47-56, 59-61, 64-76, 89, 95 and 100-102 have been amended, all without prejudice or disclaimer. Applicants submit that these claims were amended for the sole purpose of facilitating prosecution or to more clearly define the invention claimed by the Applicant. Support for the amendments is found, for example on page 96, lines 19-24, and page 97, lines 5-7. Thus, no new matter has been added by way of the amendments to the claims.

I. Withdrawn Rejections

Applicants thank the Examiner for withdrawing the rejection to claims 24-102 under 35 U.S.C. §101.

II. Examiner Interview Summary

Applicants thank the Examiner and SPE Eyler for the interview conducted on February 5, 2003. During the interview, it was indicated that the enablement rejection of claims directed to polypeptides comprising fragments of SEQ ID NO:2 in Paper No. 31 would be withdrawn if the claims were amended to recite "consisting of" instead of "comprising". *See* Interview Summary, Paper No. 32.

The Examiner and Applicants' representatives also discussed potential amendments of claims directed to variants of SEQ ID NO:2. *See* Interview Summary, Paper No. 32. It was suggested during the interview that Applicants should request reconsideration by the Examiner of the three previously submitted Declarations under 37 C.F.R. §1.132 in which use of the instant invention for either enhancing or inhibiting immune cell proliferation is supported.

As a result of the interview Applicants have prepared this amendment and response in accordance with the issues discussed during the Examiner Interview, set forth below.

III. Rejections under 35 U.S.C. §112, 1st paragraph- Enablement

A. Claims 40-42, 44-46, 50-79, 81-83 and 85-104

On page 2 of Paper No. 31, claims 40-42, 44-46, 50-79, 81-83 and 85-104 are rejected as allegedly lacking enablement. The Examiner contends that while the specification is

enabling for a polypeptide of SEQ ID NO: 2 and for polypeptides *consisting of* fragments of SEQ ID NO: 2, the specification has allegedly failed to teach polypeptides comprising only portions of or having homology to SEQ ID NO: 2.

Applicants respectfully disagree, but in the interest of facilitating prosecution, and as agreed to in the Examiner Interview discussed above, claims 40-43, and 47-53 have been amended accordingly. In view of these amendments, Applicants respectfully request reconsideration and withdrawal of the rejection with respect to these claims.

Further, on page 3 of Paper No. 31, it is asserted that, "[t]he rejection under 35 U.S.C. §101 has been withdrawn because Applicants have demonstrated that the CRCGCL functions as a cytokine [receptor], binding a cytokine and stimulating a Jak-STAT signal transduction pathway..." It is also asserted that the claimed invention is enabled for use as an activated T cell marker (due to the submission of the Rule 132 Declaration by Dr. Paul Moore on September 9, 2002). However, the claimed invention is rejected for allegedly (1) not being enabled for the other uses disclosed in the specification, and (2) encompassing a limitless number of variants.

Applicants respectfully disagree and submit that in order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the claimed polypeptides and practice a single use of the claimed polypeptides without undue experimentation. *See, e.g.,* M.P.E.P. § 2164.01(c).

This section of the MPEP also states that:

> When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. See *In re Vaeck,* 947 F.2d 488, 495, 20 USPA2d 1438, 1444 (Fed. Cir. 1991).
> In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.

See MPEP §2164.01(c) at page 2100-175 to 176.

Applicants respectfully submit that because the Patent Office recognizes that the claimed CRCGCL receptor protein: (1) functions as a cytokine [receptor], (2) binds a cytokine, (3) stimulates a Jak-STAT signal transduction pathway, and (4) is enabled for use as an activated T cell marker, these multiple uses are reasonably correlated with the entire

scope of the claimed invention, which according to the MPEP section above, is sufficient to preclude a rejection for nonenablement based on how to use.

Applicants also respectfully submit that based upon the above recognized attributes of the claimed invention, the claimed polypeptides can therefore be used to enhance or inhibit immune cell proliferation, as disclosed in the specification and as further supported by the executed Rule 132 Declarations of Dr. Paul Moore and Dr. Thi Sau Migone, submitted on September 9, 2002 and on September 26, 2001. For instance, the specification discloses and the Patent Office recognizes that the claimed CRCGCL receptor protein is homologous to the IL-2 receptor common gamma chain (*see* page 3, lines 1-5 of the specification and page 4 of Paper No. 31). As noted by Dr. Migone in section 7 of her Rule 132 Declaration, it was known in the art at the time of filing that the cytokines IL-2, IL-4, IL-7, IL-9, and IL-15 are all well-known T cell growth factors and that all these T cell growth factors use the IL-2 common gamma chain receptor. Dr. Migone also declares that:

> An immunologist, after reading [the] statements made in the 430 Application and based upon what was known in the filed of cytokine research, would understand that the 430 Application is directed to the use of the CRCGCL receptor protein as a positive regulator of T cell proliferation and would also understand that the CRCGCL receptor protein antagonist is useful for inhibiting T cell proliferation... (*see* Declaration page 6, section 17; emphasis added).

Thus, it was reasonable to Dr. Migone, a skilled artisan, that since the claimed CRCGCL receptor protein is homologous to the IL-2 common gamma chain, like the IL-2 common gamma chain, the CRCGCL receptor protein would also function as a growth factor by enhancing immune cell proliferation while an antagonist would function as an inhibitor of said proliferation.

This assertion of said biological activity by the claimed CRCGCL receptor protein was corroborated in the Rule 132 Declaration of Dr. Paul Moore submitted September 26, 2001, in which data from a 293T reconstitution cell assay and flow cytometry indicate that CRCGCL binds a cytokine and activates the Jak-STAT signal transduction pathway. The data also shows that a soluble extracellular domain of CRCGCL also binds a cytokine and inhibits the Jak-STAT pathway. As disclosed in the specification, it was well known in the art that activation of the Jak-STAT pathway is indicative of proteins able to transduce cell proliferation, particularly immune cells (*see, e.g.*, the specification at page 10, lines 23-25; and page 147, lines 6-8). Thus, this data clearly corroborates Applicants' assertions that the

claimed CRCGCL receptor can transduce immune cell proliferation and that a soluble extracellular fragment is able to act as an antagonist of said proliferation.

In view of the above, and as suggested during the Examiner Interview, claims 54-57, 59-61, 64, 76, 89, 95 and 100-102 have been amended in order to better define the claimed invention. Support for these amendments can be found throughout the specification as filed, for example on page 96, lines 19-24, and page 97, lines 5-7, therefore no new matter has been introduced. Applicants respectfully submit that according the requirements of the MPEP section quoted above, the requirements of enablement should now be evaluated based upon what is now recited in the claims in conjunction with the evidence submitted in support of enablement as discussed above.

In further support of the enablement of the newly amended claims, the specification teaches biological assays to determine if a protein proliferates immune cells (see e.g., pages 88-89, Example 14; pages 92-94, Example 17). The disclosed or otherwise known methods of making and screening polypeptides and fragments or variants thereof may be used to make and then determine, by routine experimentation, whether a given polypeptide encompassed by the claims is able to, for example, generate antagonists (including, but not limited to, for example, soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation of immune cells, or to generate CRCGCL fragments or variants which could be useful in stimulating immune cell proliferation.

On page 3 of Paper No. 31, it is further alleged that the specification has failed to teach one of skill in the art which cell types to use, if any, to regulate cell differentiation and/or proliferation. Applicants respectfully disagree and submit that the specification clearly asserts, for example, on page 96 lines 19-22 that CRCGCL polypeptides may be used to regulate the proliferation, differentiation, or mobilization of immune cells, a term of art well-understood by the skilled artisan. Nevertheless, the specification defines immune cells on page 96, lines 22-24, as:

> Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells.

On page 109, line 28, the specification reads, "For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated" (emphasis added). Thus, CRCGCL polypeptides are clearly asserted to affect the proliferation and differentiation of immune cells, particularly the hematopoetic T cells, and B cells. Furthermore, the specification also implicitly teaches

which cell types are capable of being affected by the claimed CRCGCL receptor polypeptides in that the present claimed CRCGCL receptor protein is homologous to the IL-2 common gamma chain, as discussed earlier. As stated above, the Rule 132 Declaration of Dr. Thi-Sau Migone supports the fact that this cell specificity is clearly indicated to her in the specification (*see* section 17 of Dr. Migone's Rule 132 Declaration).

The Examiner additionally maintains the allegation that the specification has not taught whether CRCGCL could be used to promote or inhibit cell differentiation and/or proliferation. Applicants disagree and submit that as discussed above, the CRCGCL receptor protein of the instant invention is homologous to the IL-2 receptor common gamma chain, and as disclosed in the specification and as noted by Dr. Migone in paragraph 7 of her Declaration, it was known in the art at the time of filing that the prior art taught that the "IL-2 common gamma chain is important for the growth and differentiation of immune cells, such as T and B lymphocytes, natural killer cells, macrophages, and monocytes." Further, IL-2, IL-4, IL-7, IL-9, and IL-15, all use the common gamma chain receptor and are all known growth factors. Thus, to Dr. Migone, it was reasonable to one of skill in the art that based upon the teachings in the specification coupled with what was known in the art (the prior art) at the time the invention was filed, the native, full length CRCGCL receptor protein would ~~also be useful in enhancing cell proliferation, just as in the IL-2 common gamma chain.~~

Additionally, upon ligand binding, the CRCGCL receptor activates the Jak-STAT pathway, such pathway activation being indicative of proteins involved in cell proliferation (as disclosed on page 147, lines 6-9 of the specification and as further corroborated by the data presented in Dr. Paul Moore's Rule 132 Declaration submitted on July 26, 2001). This fact is noted in Dr. Migone's Rule 132 Declaration in paragraphs 8 and 9 and indicated to her that the claimed CRCGCL receptor protein would be involved in cell proliferation and differentiation. Furthermore, expression of the CRCGCL receptor in activated T cells as opposed to resting T cells additionally supports a role for the CRCGCL receptor in immune cell proliferation rather than the inhibition of proliferation (*see* Dr. Paul Moore's Rule 132 Declaration submitted on September 9, 2002). Applicants reiterate that in her Rule 132 Declaration, Dr. Migone declares that based on the teachings in the specification combined with what was known in the art, one would understand after reading the specification that the 430 Application is directed to the use of the CRCGCL receptor protein as a positive regulator of T cell proliferation, and one would also understand that the CRCGCL receptor protein antagonist is useful for inhibiting T cell proliferation (*see* Declaration page 6, paragraph 17).

In light of the above, and the discussion during the February 5, 2003 interview, Applicants believe that the rejections under 35 U.S.C. § 112, first paragraph, made in Paper No. 31 have been overcome. Accordingly, Applicants respectfully request that the pending rejections be reconsidered and withdrawn.

IV. Rejections under 35 U.S.C. §112, 1st paragraph- Written Description

On page 5, paragraph 3.2 of Paper No. 31, claims 40-42, 44-46, 50-79, 81-83 and 85-104 are rejected as allegedly lacking written description. Applicants respectfully disagree, and maintain that the specification clearly teaches to one of skill in the art the variants and fragments contemplated as encompassed within the claimed invention (*see* Applicants' previous response, pages 11-12).

However, as discussed above, to facilitate prosecution, claims 40-43, 47-56, 59-61, 64-76, 89, 95 and 100-102 have been amended as suggested in the Examiner Interview (*see* Examiner Interview Summary, Paper No. 32). Specifically, claims 40-42, 50-53 have been amended to recite "consisting of" language, and claims 54-56, 59-61, 64, 76, 89, 95 and 100-102 have been amended to recite that the claimed polypeptides transduce (or inhibit for some of the claims) immune cell (or hematopoietic cell) proliferation. These amendments are fully supported in the specification, for instance on pages 96, lines 19-24 and page 97, lines 5-7 and supported as discussed above. Thus, no new matter has been added and entry of the amended claims is respectfully requested.

The MPEP §2163 advises that the written description requirement is satisfied, "by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *See* page 2100-161 of MPEP § 2163, eighth edition (2001). Applicants respectfully submit that not only is the full-length amino acid sequence of the claimed invention disclosed (as SEQ ID NO: 2), the specification also discusses the various consensus domains of the claimed protein as compared to its closest homolog, the IL-2 common gamma chain, thereby linking structure with function (*see* page 9, lines 8-25 and Figure 2 of the specification). Therefore, one of skill in the art would know which domains of the claimed invention should remain untouched in order to generate the fragments and variants encompassed within the scope of the newly amended claims.

In light of the above amendments, Applicants believe that the rejections under 35 U.S.C. § 112, first paragraph, made in Paper No. 31 have been overcome and respectfully request that the pending rejections be reconsidered and withdrawn.

V. Rejections under 35 U.S.C. §112, 2nd paragraph- Indefiniteness

A. Claims 43, 48 and 49

On page 6 of Paper No. 31, claims 43, 48 and 49 have been rejected for reciting the limitation "amino acid sequence (c)" for which there is no antecedent basis. Applicants submit that these claims depend from claim 40, which has been amended to include a subpart (c), thus dependent claims 43 and 48 are now proper. Additionally, claim 49 has been amended and no longer depends from claim 40, overcoming this rejection. As such, Applicants respectfully request that this rejection be reconsidered and withdrawn.

B. Claims 80 and 84

On page 6 of Paper No. 31, claims 80 and 84 have been rejected for reciting the limitation "amino acid sequence (d)" for which there is no antecedent basis. Applicants have canceled these claims, thus this rejection has been rendered moot.

~~*VI. Objection to Claim 47*~~

Claim 47 is objected to as being dependent upon previously rejected claim 42. As discussed above, Applicants note that claims 42 and 40 (from which claim 42 depends) have been amended to recite "consisting of" language. Thus Applicants believe that they are now in condition for allowance, and that claim 47 should now be allowable as well. As such, Applicants respectfully request that the Examiner reconsider this objection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: February 15, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Moore et al.

Application Serial No.: 09/376,430 — Art Unit: 1646

Filed: August 18, 1999 — Examiner: O'Hara, E.

For: **Cytokine Receptor Common Gamma Chain Like** — Attorney Docket No.: PF466P1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

40. (Amended Three Times) An isolated polypeptide ~~having immune cell proliferative activity comprising~~ consisting of an amino acid sequence selected from the group consisting of:

(a) amino acid residues m to 371 of SEQ ID NO:2, where m is an integer in the range of ~~+2~~ +1 to +370; ~~and~~

(b) amino acid residues 1 to n of SEQ ID NO:2, where n is an integer in the range of +2 to +371; and

(c) amino acid residues m to n of SEQ ID NO:2, where m is an integer in the range of +1 to +370 and n is an integer in the range of +2 to 371;

wherein said amino acid sequence ~~comprises~~ consists of at least seven contiguous amino acid residues of SEQ ID NO:2.

41. (Once Amended) The isolated polypeptide of claim 40, which ~~comprises~~ consists of amino acid sequence (a).

42. (Once Amended) The isolated polypeptide of claim 40, which ~~comprises~~ consists of amino acid sequence (b).

43. (Once Amended) The isolated polypeptide of claim 40, which ~~comprises~~ consists of amino acid sequence (c).

47. (Once Amended) The isolated polypeptide of claim 42, wherein said amino acid sequence ~~comprises~~ consists of amino acid residues +1 to +231 of SEQ ID NO:2.

48. (Once Amended) The isolated polypeptide of claim 43, wherein said amino acid sequence ~~comprises~~ consists of amino acid residues selected from the group consisting of:

(a) amino acid residues +23 to +231 of SEQ ID NO:2;

(b) amino acid residues +23 to +225 of SEQ ID NO:2; and

~~(c) amino acid residues +198 to +204 of SEQ ID NO:2;~~

~~(d)~~ (c) amino acid residues +226 to +260 of SEQ ID NO:2. ~~; and~~

~~(e) amino acid residues +261 to +268 of SEQ ID NO:2.~~

49. (Once Amended) ~~The~~ An isolated polypeptide ~~of claim 43, wherein said amino acid sequence comprises amino acid residues~~ consisting of an amino acid sequence selected from the group consisting of:

(a) amino acid residues +22 to +29 of SEQ ID NO:2;

(b) amino acid residues +48 to +56 of SEQ ID NO:2;

(c) amino acid residues +62 to +73 of SEQ ID NO:2;

(d) amino acid residues +78 to +85 of SEQ ID NO:2;

(e) amino acid residues +88 to +95 of SEQ ID NO:2;

(f) amino acid residues +99 to +105 of SEQ ID NO:2;

(g) amino acid residues +118 to +126 of SEQ ID NO:2;

(h) amino acid residues +139 to +146 of SEQ ID NO:2;

(i) amino acid residues +151 to +169 of SEQ ID NO:2;

(j) amino acid residues +188 to +206 of SEQ ID NO:2;

(k) amino acid residues +208 to +231 of SEQ ID NO:2;

(l) amino acid residues +264 to +271 of SEQ ID NO:2;

(m) amino acid residues +286 to +293 of SEQ ID NO:2;

(n) amino acid residues +300 to +313 of SEQ ID NO:2;

(o) amino acid residues +317 to +342 of SEQ ID NO:2;

(p) amino acid residues +347 to +353 of SEQ ID NO:2; and

(q) amino acid residues +363 to +369 of SEQ ID NO:2;

wherein the polypeptide consisting of said amino acid sequence is fused to a heterologous polypeptide.

50. (Twice Amended) An isolated polypeptide ~~comprising~~ consisting of at least 30 contiguous amino acid residues of SEQ ID NO:2.~~, wherein said polypeptide inhibits immune cell proliferation.~~

51. (Twice Amended) An isolated polypeptide ~~comprising~~ consisting of at least 30 contiguous amino acid residues encoded by the cDNA in ATCC Deposit No. 209691 or 209641.~~, wherein said polypeptide inhibits immune cell proliferation.~~

52. (Once Amended) The isolated polypeptide of claim 50, ~~further comprising~~ consisting of at least 50 contiguous amino acid residues of SEQ ID NO:2.

53. (Once Amended) The isolated polypeptide of claim 51, ~~further comprising~~ consisting of at least 50 amino acid residues encoded by the cDNA in ATCC Deposit No. 209691 or 209641.

54. (Once Amended) The isolated polypeptide of claim 50 wherein said polypeptide ~~regulates~~ inhibits the differentiation and/or proliferation of immune cells.

55. (Once Amended) The isolated polypeptide of claim 50 wherein said polypeptide ~~stimulates proliferation or differentiation of immune cells.~~ transduces immune cell proliferation.

56. (Once Amended) The isolated polypeptide of claim 50 wherein said polypeptide ~~stimulates proliferation or differentiation of hematopoietic cells.~~ transduces hematopoietic cell proliferation.

59. (Once Amended) The isolated polypeptide of claim 51 wherein said polypeptide ~~regulates~~ inhibits the differentiation and/or proliferation of immune cells.

60. (Once Amended) The isolated polypeptide of claim 51 wherein said polypeptide ~~stimulates proliferation or differentiation of immune cells.~~ transduces immune cell proliferation.

61. (Once Amended) The isolated polypeptide of claim 51 wherein said polypeptide ~~stimulates proliferation or differentiation of hematopoietic cells.~~ transduces hematopoietic cell proliferation.

64. (Once Amended) An isolated polypeptide comprising a first amino acid sequence 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) amino acids +1 to +371 of SEQ ID NO:2;

(b) amino acids +2 to +371 of SEQ ID NO:2;

(c) amino acids +23 to +371 of SEQ ID NO:2; and

(d) amino acids +23 to +231 of SEQ ID NO:2;

wherein the isolated polypeptide comprising said first amino acid sequence ~~has immune cell proliferative activity.~~ transduces immune cell proliferation.

76. (Once Amended) An isolated polypeptide comprising a first amino acid sequence 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) an amino acid sequence of the full length polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(b) an amino acid sequence of the full length polypeptide, excluding the N-terminal methionine residue, encoded by the cDNA in ATCC Deposit No. 209691 or 209641; and

(c) an amino acid sequence of the mature polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

wherein the polypeptide comprising said first amino acid sequence ~~has immune cell proliferative activity.~~ transduces immune cell proliferation.

89. (Once Amended) The isolated polypeptide of claim 88 which ~~regulates~~ transduces the differentiation and/or proliferation of immune cells.

95. (Once Amended) The isolated polypeptide of claim 94 which ~~regulates~~ transduces the differentiation and/or proliferation of immune cells.

100. (Once Amended) An isolated polypeptide comprising an amino acid sequence, wherein, except for one to 30 amino acid substitutions, said amino acid sequence is identical to contiguous amino acid residues selected from the group consisting of:

(a) amino acid residues +1 to +371 of SEQ ID NO:2;

(b) amino acids residues +2 to +371 of SEQ ID NO:2;

(c) amino acids residues +23 to +371 of SEQ ID NO:2; and

(d) amino acids residues +23 to +231 of SEQ ID NO:2;

wherein said isolated polypeptide ~~has immune cell proliferative activity.~~ transduces immune cell proliferation.

101. (Once Amended) An isolated polypeptide comprising an amino acid sequence, wherein, except for one to 30 amino acid substitutions, said amino acid sequence is identical to contiguous amino acid residues selected from the group consisting of:

(a) an amino acid sequence of the full length polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(b) an amino acid sequence of the full length polypeptide, excluding the N-terminal methionine residue, encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(c) an amino acid sequence of the mature polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

(d) an amino acid sequence of the extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641; and

(e) an amino acid sequence of the soluble extracellular domain of the polypeptide encoded by the cDNA in ATCC Deposit No. 209691 or 209641;

wherein said isolated polypeptide ~~has immune cell proliferative activity~~ transduces immune cell proliferation.

102. (Once Amended) An isolated protein comprising a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of amino acid residues +1 to +371 of SEQ ID NO:2, in which 1 or more amino acid residues are substituted, deleted or added, in any combination

and wherein said polypeptide ~~has immune cell proliferative activity; and~~ transduces immune cell proliferation;

(b) a polypeptide consisting of a fragment of SEQ ID NO:2 which fragment ~~has immune cell proliferative activity.~~ transduces immune cell proliferation; and

(c) a polypeptide consisting of a fragment of SEQ ID NO:2 which fragment inhibits immune cell proliferation.